To: WRITTEN OPINION OF THE see form PCT/ISA/220 INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1) Date of mailing (day/month/year) see form PCT/ISA/210 (second sheet) Applicant's or agent's file reference FOR FURTHER ACTION see form PCT/ISA/220 See paragraph 2 below International application No. International filing date (day/month/year) Priority date (day/month/year) PCT/EP2005/002477 08.03.2005 29.12.2004 International Patent Classification (IPC) or both national classification and IPC A61K7/48 Applicant LABO COSPROPHAR AG 1. This opinion contains indications relating to the following items: Box No. 1 Basis of the opinion ☐ Box No. II ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability ☐ Box No. IV Lack of unity of invention Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement ☐ Box No. VI Certain documents cited ☐ Box No. VII Certain defects in the international application ☐ Box No. VIII Certain observations on the international application 2. **FURTHER ACTION** If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1 bis(b) that written opinions of this International Searching Authority will not be so considered. If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later. For further options, see Form PCT/ISA/220. For further details, see notes to Form PCT/ISA/220.

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY



	Во	x N	lo. I	Basis of the opinion
1.				to the language, this opinion has been established on the basis of the international application in the international application in the language, this opinion has been established on the basis of the international application in the language, this opinion has been established on the basis of the international application in the language, this opinion has been established on the basis of the international application in the language, this opinion has been established on the basis of the international application in the language.
		la	ngua	pinion has been established on the basis of a translation from the original language into the following ge , which is the language of a translation furnished for the purposes of international search Rules 12.3 and 23.1(b)).
2.		th regard to any nucleotide and/or amino acid sequence disclosed in the international application and cessary to the claimed invention, this opinion has been established on the basis of:		
	a. t	ype	of m	naterial:
		Ø	a se	equence listing
			table	le(s) related to the sequence listing
	b. f	orm	nat of	f material:
		Ø	in w	vritten format
		×	in c	omputer readable form
	c. t	ime	of fil	ling/furnishing:
			con	tained in the international application as filed.
			filed	d together with the international application in computer readable form.
		×	furn	nished subsequently to this Authority for the purposes of search.
3.	×	ha cc	as be opies	ition, in the case that more than one version or copy of a sequence listing and/or table relating theretoen filed or furnished, the required statements that the information in the subsequent or additional is identical to that in the application as filed or does not go beyond the application as filed, as priate, were furnished.

4. Additional comments:

Box No. V Reasoned statement under Rule 43bis.1(a)(l) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)

Yes: Claims

1-21

No: Claims

Inventive step (IS)

Yes: Claims

3-4,8-9,13-14

No: Claims

1-2,5-7,10-12,15-21

Industrial applicability (IA)

Yes: Claims

1-21

No: Claims

2. Citations and explanations

see separate sheet

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AP20 Roof CPC 1270 21 JUN 2006

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

- 1. Reference is made to the following documents:
- D1: "COSMETIC ALTERNATIVES TO BOTOX KOSMETISCHE ALTERNATIVEN ZU BOTOX" COSSMA: COSMETICS, SPRAY TECHNOLOGY, MARKETING, vol. 5, no. 11, 2004, pages 28-29
- D2: ANONYMOUS: "Muscle relaxant peptide" RESEARCH DISCLOSURE, vol. 478, no. 11, February 2004 (2004-02)
- D3: EP-A-1 155 686 (L'OREAL)
- D4: "ACTIVE POWER FROM PEPTIDES" COSSMA: COSMETICS, SPRAY TECHNOLOGY, MARKETING, vol. 5, no. 11, 2004, pages 30-31
- 2. None of the prior art documents discloses a cosmetic composition for relaxing expression wrinkle comprising a combination of a myorelaxant peptide and a microelement which reduces the contraction of muscular fibres.

The subject matter of independent claims 1 and 19, as well as that of dependent claims 2-18 and 20-21 is novel over the prior art (Art. 33(2 PCT).

3. The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1 and 19 does not involve an inventive step in the sense of Article 33(3) PCT.

Prior art documents D1-D4 disclose the use of myorelaxant compositions for treating expression wrinkles. More specifically:

D1 is a review article disclosing cosmetic alternatives to Botox, such as oligopeptides or plant extracts. The wrinkle reducing action of anise extracts, magnesium gluconate, as well as the curare-like acting pentapeptidamine-4 peptide (Pentapharm's Vialox) are mentioned.

D2 discloses the use of the dipeptide Tyr-Arg in cosmetics for smoothing out expression wrinkles.

D3 discloses the use of magnesium salts, especially magnesium gluconate for the same purpose.

D4 discloses the use of peptides such as the dipeptides Calmosensine (Tyr-Arg), Eyeliss (Val-Trp), the pentapeptides Matrixyl (Lys-Thr-Thr-Lys-Ser) and pentapeptidamine-4 peptide (Pentapharm's Vialox), in the treatment of expression wrinkles.

The subject-matter of claims 1 and 19 differs from the prior art in that a combination composition of a myorelaxant peptide and a myorelaxant microelement is used. The problem to be solved can thus be seen as providing alternative compositions for treating expression wrinkles.

In view of prior art documents D1-D4, it is considered that the solution proposed, namely the use of a combination product is not inventive. The individual part compounds of the combination product are already used in cosmetics for treating wrinkles. Combining these does not involve the exercise of an inventive skill, especially since the known myorelaxant properties of the compounds are used. An inventive step could be acknowledged in case of a synergistic effect. No such effect has been shown.

- **4.** Dependent claims 2, 5-7, 10-12, 15-21 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of inventive step, see documents D1-D4 and the corresponding passages cited in the search report.
- **6.** The combination of the features of dependent claims 3-4, 8-9, 13-14 is neither known from, nor rendered obvious by, the available prior art, since no prior art document discloses the use of the pentapeptide Gly-Pro-Arg-Pro-Ala in cosmetics. The subject matter of these claims meets the requirements of novelty and inventive step.
- 7. The term "micro-element which reduces the contraction of a muscular fibre" used in claims 1 and 19 is vague and unclear and leaves the reader in doubt as to the meaning of the technical features to which it refers, thereby rendering the definition of the subject-matter of said claim/s unclear, Article 6 PCT.

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (SEPARATE SHEET)

International application No.

PCT/EP2005/002477